



SEQUENCE LISTING

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<120> HEPARANASE ACTIVITY NEUTRALIZING ANTI-HEPARANASE MONOCLONAL
ANTIBODY AND OTHER ANTI-HEPARANASE ANTIBODIES

<130> 30337

<160> 14

<170> PatentIn version 3.5

<210> 1
<211> 386
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> 45 kDa subunit of mature processed heparanase dimer

<400> 1

Lys Lys Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu
1 5 10 15

Tyr Thr Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn
20 25 30

Ala Leu Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln
35 40 45

Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu
50 55 60

Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile
65 70 75 80

Asn Gly Ser Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu
85 90 95

Arg Lys Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly
100 105 110

Gln Pro Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala
115 120 125

Gly Gly Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn
130 135 140

Gly Arg Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp

145 150 155 160
 Ile Phe Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr
 165 170 175
 Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly
 180 185 190
 Gly Gly Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp
 195 200 205
 Leu Asp Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met
 210 215 220
 Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn
 225 230 235 240
 Phe Asp Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu
 245 250 255
 Val Gly Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg
 260 265 270
 Lys Leu Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr
 275 280 285
 Lys Glu Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr
 290 295 300
 Lys Tyr Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys
 305 310 315 320
 Tyr Leu Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val
 325 330 335
 Gln Leu Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro
 340 345 350
 Pro Leu Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro
 355 360 365
 Ala Phe Ser Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala
 370 375 380
 Cys Ile
 385
 <210> 2
 <211> 535
 <212> PRT
 <213> Mus musculus
 <400> 2
 Met Leu Arg Leu Leu Leu Leu Trp Leu Trp Gly Pro Leu Gly Ala Leu

1	5	10	15
Ala Gln Gly	Ala Pro Ala Gly Thr	Ala Pro Thr Asp Asp	Val Val Asp
	20	25	30
Leu Glu Phe Tyr Thr Lys Arg	Pro Leu Arg Ser Val Ser	Pro Ser Phe	
	35	40	45
Leu Ser Ile Thr Ile Asp	Ala Ser Leu Ala Thr Asp	Pro Arg Phe Leu	
	50	55	60
Thr Phe Leu Gly Ser	Pro Arg Leu Arg Ala	Leu Ala Arg Gly Leu Ser	
	65	70	75
Pro Ala Tyr Leu Arg Phe Gly Gly Thr	Lys Thr Asp Phe Leu	Ile Phe	
	85	90	95
Asp Pro Asp	Lys Glu Pro Thr Ser	Glu Glu Arg Ser Tyr Trp Lys Ser	
	100	105	110
Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val			
	115	120	125
Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu			
	130	135	140
Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser			
	145	150	155
Ser Val Asp Met	Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu		
	165	170	175
Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn			
	180	185	190
Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr			
	195	200	205
Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys			
	210	215	220
Ala His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu			
	225	230	235
Leu His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr			
	245	250	255
Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg			
	260	265	270
Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His			
	275	280	285

His Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser
290 295 300

Ser Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys
305 310 315 320

Val Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr
325 330 335

Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala
340 345 350

Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly
355 360 365

Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His
370 375 380

Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu
385 390 395 400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys
405 410 415

Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val
420 425 430

Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn
435 440 445

Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg
450 455 460

Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu
465 470 475 480

Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp
485 490 495

Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser
500 505 510

Ala Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn
515 520 525

Ala Lys Ile Ala Ala Cys Ile
530 535

<210> 3

<211> 536

<212> PRT

<213> Rattus norvegicus

<400> 3

Met Leu Arg Pro Leu Leu Leu Trp Leu Trp Gly Arg Leu Arg Ala
 1 5 10 15
 Leu Thr Gln Gly Thr Pro Ala Gly Thr Ala Pro Thr Lys Asp Val Val
 20 25 30
 Asp Leu Glu Phe Tyr Thr Lys Arg Leu Phe Gln Ser Val Ser Pro Ser
 35 40 45
 Phe Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe
 50 55 60
 Leu Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu
 65 70 75 80
 Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile
 85 90 95
 Phe Asp Pro Asn Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Gln
 100 105 110
 Ser Gln Asp Asn Asn Asp Ile Cys Gly Ser Glu Arg Val Ser Ala Asp
 115 120 125
 Val Leu Arg Lys Leu Gln Met Glu Trp Pro Phe Gln Glu Leu Leu Leu
 130 135 140
 Leu Arg Glu Gln Tyr Gln Arg Glu Phe Lys Asn Ser Thr Tyr Ser Arg
 145 150 155 160
 Ser Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Arg Leu Asp
 165 170 175
 Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp
 180 185 190
 Asn Ser Ser Asn Ala Gln Leu Leu Leu Asn Tyr Cys Ser Ser Lys Gly
 195 200 205
 Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys
 210 215 220
 Lys Ala Gln Ile Ser Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val
 225 230 235 240
 Glu Leu His Lys Leu Leu Gln Lys Ser Ala Phe Gln Asn Ala Lys Leu
 245 250 255
 Tyr Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu
 260 265 270
 Arg Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp
 275 280 285

His His Tyr Tyr Leu Asn Gly Arg Val Ala Thr Lys Glu Asp Phe Leu
290 295 300

Ser Ser Asp Val Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu
305 310 315 320

Lys Val Thr Lys Glu Met Thr Pro Gly Lys Lys Val Trp Leu Gly Glu
325 330 335

Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe
340 345 350

Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Leu
355 360 365

Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr
370 375 380

His Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser
385 390 395 400

Leu Leu Phe Lys Lys Leu Val Gly Pro Lys Val Leu Met Ser Arg Val
405 410 415

Lys Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn
420 425 430

Val Tyr His Pro Arg Tyr Arg Glu Gly Asp Leu Thr Leu Tyr Val Leu
435 440 445

Asn Leu His Asn Val Thr Lys His Leu Lys Leu Pro Pro Pro Met Phe
450 455 460

Ser Arg Pro Val Asp Lys Tyr Leu Leu Lys Pro Phe Gly Ser Asp Gly
465 470 475 480

Leu Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Thr Leu Lys Met Val
485 490 495

Asp Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly
500 505 510

Ser Ser Leu Ser Val Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg
515 520 525

Asn Ala Lys Ile Ala Ala Cys Ile
530 535

<210> 4
<211> 543
<212> PRT
<213> Homo sapiens

<400> 4

Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu Leu
1 5 10 15
Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro
20 25 30
Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
35 40 45
Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
50 55 60
Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65 70 75 80
Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
85 90 95
Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe
100 105 110
Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys
115 120 125
Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp
130 135 140
Pro Tyr Gln Glu Gln Leu Leu Arg Glu His Tyr Gln Lys Lys Phe
145 150 155 160
Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
165 170 175
Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
180 185 190
Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
195 200 205
Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn
210 215 220
Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
225 230 235 240
Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser
245 250 255
Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
260 265 270
Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
275 280 285

Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
290 295 300

Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
305 310 315 320

Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly
325 330 335

Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala
340 345 350

Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys
355 360 365

Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val
370 375 380

Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro
385 390 395 400

Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
405 410 415

Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
420 425 430

Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
435 440 445

Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
450 455 460

Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu
465 470 475 480

Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn
485 490 495

Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met
500 505 510

Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
515 520 525

Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
530 535 540

<210> 5
<211> 523
<212> PRT
<213> Gallus gallus

<400> 5

Met Leu Val Leu Leu Leu Val Leu Leu Leu Ala Val Pro Pro Arg
1 5 10 15

Arg Thr Ala Glu Leu Gln Leu Gly Leu Arg Glu Pro Ile Gly Ala Val
20 25 30

Ser Pro Ala Phe Leu Ser Leu Thr Leu Asp Ala Ser Leu Ala Arg Asp
35 40 45

Pro Arg Phe Val Ala Leu Leu Arg His Pro Lys Leu His Thr Leu Ala
50 55 60

Ser Gly Leu Ser Pro Gly Phe Leu Arg Phe Gly Gly Thr Ser Thr Asp
65 70 75 80

Phe Leu Ile Phe Asn Pro Asn Lys Asp Ser Thr Trp Glu Glu Lys Val
85 90 95

Leu Ser Glu Phe Gln Ala Lys Asp Val Cys Glu Ala Trp Pro Ser Phe
100 105 110

Ala Val Val Pro Lys Leu Leu Leu Thr Gln Trp Pro Leu Gln Glu Lys
115 120 125

Leu Leu Leu Ala Glu His Ser Trp Lys Lys His Lys Asn Thr Thr Ile
130 135 140

Thr Arg Ser Thr Leu Asp Ile Leu His Thr Phe Ala Ser Ser Ser Gly
145 150 155 160

Phe Arg Leu Val Phe Gly Leu Asn Ala Leu Leu Arg Arg Ala Gly Leu
165 170 175

Gln Trp Asp Ser Ser Asn Ala Lys Gln Leu Leu Gly Tyr Cys Ala Gln
180 185 190

Arg Ser Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe
195 200 205

Arg Lys Lys Ser Gly Ile Cys Ile Asp Gly Phe Gln Leu Gly Arg Asp
210 215 220

Phe Val His Leu Arg Gln Leu Leu Ser Gln His Pro Leu Tyr Arg His
225 230 235 240

Ala Glu Leu Tyr Gly Leu Asp Val Gly Gln Pro Arg Lys His Thr Gln
245 250 255

His Leu Leu Arg Ser Phe Met Lys Ser Gly Gly Lys Ala Ile Asp Ser
260 265 270

Val Thr Trp His His Tyr Tyr Val Asn Gly Arg Ser Ala Thr Arg Glu

275	280	285
Asp Phe Leu Ser Pro Glu Val Leu Asp Ser Phe Ala Thr Ala Ile His 290 295 300		
Asp Val Leu Gly Ile Val Glu Ala Thr Val Pro Gly Lys Lys Val Trp 305 310 315 320		
Leu Gly Glu Thr Gly Ser Ala Tyr Gly Gly Gly Ala Pro Gln Leu Ser 325 330 335		
Asn Thr Tyr Val Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ala 340 345 350		
Ala Arg Arg Gly Ile Asp Val Val Met Arg Gln Val Ser Phe Gly Ala 355 360 365		
Gly Ser Tyr His Leu Val Asp Ala Gly Phe Lys Pro Leu Pro Asp Tyr 370 375 380		
Trp Leu Ser Leu Leu Tyr Lys Arg Leu Val Gly Thr Arg Val Leu Gln 385 390 395 400		
Ala Ser Val Glu Gln Ala Asp Ala Arg Arg Pro Arg Val Tyr Leu His 405 410 415		
Cys Thr Asn Pro Arg His Pro Lys Tyr Arg Glu Gly Asp Val Thr Leu 420 425 430		
Phe Ala Leu Asn Leu Ser Asn Val Thr Gln Ser Leu Gln Leu Pro Lys 435 440 445		
Gln Leu Trp Ser Lys Ser Val Asp Gln Tyr Leu Leu Leu Pro His Gly 450 455 460		
Lys Asp Ser Ile Leu Ser Arg Glu Val Gln Leu Asn Gly Arg Leu Leu 465 470 475 480		
Gln Met Val Asp Asp Glu Thr Leu Pro Ala Leu His Glu Met Ala Leu 485 490 495		
Ala Pro Gly Ser Thr Leu Gly Leu Pro Ala Phe Ser Tyr Gly Phe Tyr 500 505 510		
Val Ile Arg Asn Ala Lys Ala Ile Ala Cys Ile 515 520		

<210> 6
 <211> 10
 <212> PRT
 <213> Artificial sequence

 <220>
 <223> Functional peptide epitope of heparanase

<400> 6

Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys
1 5 10

<210> 7

<211> 19

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 7

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe
1 5 10 15

Asp Pro Lys

<210> 8

<211> 15

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 8

Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala
1 5 10 15

<210> 9

<211> 15

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 9

Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr
1 5 10 15

<210> 10

<211> 14

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 10

Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg
1 5 10

<210> 11

<211> 74

<212> PRT

<213> Homo sapiens

<220>
 <221> misc_feature
 <223> 8 kDa subunit of mature processed heparanase dimer

 <400> 11

 Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro Leu His Leu
 1 5 10 15

 Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala Thr
 20 25 30

 Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu Arg Thr Leu
 35 40 45

 Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr
 50 55 60

 Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu
 65 70

<210> 12
 <211> 6
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> A conserved basic amino acid cluster (residues 157-162 of the
 human heparanase)

 <400> 12

Gln Lys Lys Phe Lys Asn
 1 5

<210> 13
 <211> 8
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> A conserved basic amino acid cluster (residues 271-278 of the
 human heparanase)

 <400> 13

Pro Arg Arg Lys Thr Ala Lys Met
 1 5

<210> 14
 <211> 8
 <212> PRT
 <213> Homo sapiens

<220>
 <221> misc_feature
 <223> A conserved basic amino acid cluster (residues 426-433 of the
 human heparanase)

<400> 14

Ser Lys Arg Arg Lys Leu Arg Val
1 5